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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,016	10/31/2003	Roberto Latini	2503-1036-1	1104

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EXAMINER	
CHEU, CHANGHWA J	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 02/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/697,016	LATINI ET AL.	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

Written Description

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claim 1-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Cerebral Ictus disease

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

The instant invention directs to a method for prognosis of myocardial infarction or cerebral ictus patients. The recited method mainly comprises measuring the PTX3 levels from the blood or plasma samples from these patients.

However, the specification merely supports the results of myocardial infarction, *NOT* for the cerebral ictus prognosis.

Examiner would like to direct application's attention to the results of the clinical analysis of the patients. The samples are from having symptoms of heart problem and some of

them died during the two months following infarction and some were affected by a new ischemic or heart failure episode (See page 5, Example 2-Clinical Study).

The results are shown in Figure 1-3 (Figure 3 is a biostatisical analysis). Particularly, there is NO clinical data for cerebral ictus. Figure 1 shows five categories of patients, including (1) healthy control, (2) heart failure, (3) ischemica, (4) both ischemia and heart failure and (5) death. The results show the level of PTX3 in all these five categories patients, NOT included cebral ictus (emphasis added).

Since the disclosure fails to describe the actual clinical confirmation of the relationship of cerebral ictus and the level of PTX3, one of skill in the art would reasonably conclude that applicant does not possess the recited invention method.

Scope of Enablement

Cerebral Ictus disease

3. Claim 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for prognosis of myocardial infarction, does not reasonably provide enablement for cerebral ictus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

As has been discussed before, the instant specification does not disclose the clinical data of cerebral ictus. In view of the aforementioned lack of predictability in the art, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in the applicant's specification of how to effectively practice the recited method and absent working examples.

PTX3 Reference level

4. Claim 2-3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for prognosis of myocardial infarction, does not reasonably provide enablement for cerebral ictus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim 2 and 3 recites the PTX3 reference concentration value is 2 and 5 ng/ml. These two values are used to compare the level of potential myocardial infraction patients for prognosis indicator.

Examiner would like to draw application's attention to the clinical analysis results, especially Figure 1.

Figure 1 shows the levels of PTX3 plasma levels in different categories of patients. The first bar is the healthy control one. The level of PTX3 in the control one is 7.80 ng/ml which is greater than 2 or 5 mg/ml as recited in claim 2-3. Furthermore, no other category, such as death or ischemia is lower than this cutting level (See fourth or last bar). It is concluded that the pathological symptoms, such as the instant recited myocardial infraction, needs to exceed this level, i.e. 7.08 ng/ml for affirmation of diagnosis. Accordingly, instead of setting limitation on either 2 or 5 ng/ml, the scope of enablement threshold should be at least more than 7.08 ng/ml as supported in the specification Figure 1.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to the term PTX3, it is unclear about this term. Applicant needs to clearly spell it for clarity.

With respect to claim 1, step (c), it is not clear about this comparing step, particularly with a reference where the reference concentration is equal to or higher than the healthy control subjects. It is not clear what constitutes "higher" and how high is "an *increased* PTX3 concentration in the sample"(emphasis added). In another word, the recited language could mean that the tested sample having the same concentration of the reference yet is 3-10 fold higher than the control and still be considered normal. Applicant needs to clarify.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claim 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peri et al. (Circulation 2000 Vol. 102, page 636 as discussed in the specification).

Peri et al. disclose that the PTX3 is a good biomarker for acute myocardial infarction (See Abstract and Conclusion). Peri et al. measure the levels of PTX3 from the patients suffered myocardial infarction and discovered the correlation between the elevated of PTX3 in plasma or blood with the myocardial infarction patients (See Methods, Figure 1 and Figure 2).

The results of Peri's analysis show that PTX3 is an indicator for diagnosis of myocardial infarction. However, Peri et al. do not explicitly teach the PTX3 plasma level is an indicator for prognosis of myocardial infarction.

Nevertheless, Peri et al. also examined morphological myocardial samples from patients who died after myocardial infarction, namely *prognosis*, by using anti-PTX3 antibody staining (See Method and Figure 4-6). The results show that some "myoctes bordering the infarcted zone similar to that senn in the normal or hypertrophied myocardium was evident" (See Figure 5, bottom).

Given the fact that prognosis is a prospective development of a disease, it would have been obvious to one ordinary skill in the art at the time the invention was made to have

motivated one to further quantitate PTX3 for the prognosis development of myocardial infarction with reasonable expectation of success as suggested in Peri et al. since it is evident from Peri et al that PTX3 plays important role in myocardial infarction, and the final autopsy (end of prognosis) suggested link with PTX3 levels in the target myocardial cells.

With respect to claim 2-3, Peri et al. report that the cutting off value for PTX3 is at least 2ng/ml (See page 638, left column, first paragraph).

With respect to claim 4-5, Peri et al. teach using ELISA to measure PTX3 (See page 637, right column, Assay section).

With respect to claim 6, Peri et al. teach measuring early heart failure, e.g. 24 hour (See Method).

With respect to claim 10, the limitations described for the PTX3 antibodies and detection reagents in a kit, would appear to be an obvious expedient for ease and convenience in assay performance.

Conclusion

10. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-272-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jacob Cheu
Examiner
Art Unit 1641

February 9, 2006

LONG V. LE
SUPERVISORY PATENT EXAMINER
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02/10/06